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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/611,432	07/02/2003	Don C. Rockey	1579-836	8031

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EXAMINER
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WHITEMAN, BRIAN A

ART UNIT	PAPER NUMBER
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1635

DATE MAILED: 12/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/611,432	ROCKEY, DON C.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Brian Whiteman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 14 November 2005.
- 2a) ☐ This action is FINAL.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-7 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-7 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 02 July 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                        | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)               | Paper No(s)/Mail Date. _____  |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>7/2/03</u> .  | 6) <input type="checkbox"/> Other: _____                                    |

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## **DETAILED ACTION**

### **Non-Final Rejection**

Claims 1-7 are pending.

### ***Election/Restrictions***

Applicant's election without traverse of adenovirus in the reply filed on 11/14/05 is acknowledged.

Retroviral and adeno-associated virus in claim 5 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 11/14/05.

### ***Priority***

The status of the parent application needs updated in the instant specification.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 3-7 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant

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art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1 and 3-7, as best understood, are readable on a genus of a nucleic acid sequence encoding a polypeptide having nitric oxide synthase (NOS) activity, wherein the genus of the nucleic acid sequences are not claimed in a specific biochemical or molecular structure that could be envisioned by one skilled in the art at the time the invention was made are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification contemplates production of a genus of a nucleic acid sequence encoding a polypeptide having NOS activity. The specification and the art of record provide sufficient description of a species of a nucleic acid sequences encoding a polypeptide having a NOS activity, the NOS polypeptide (pages 2-3). However, the specification does not teach the skilled artisan how to make a genus of nucleic acids encoding a polypeptide having a NOS activity. The specification does not disclose a structure-function correlation between NOS polypeptide and the claimed genus. It is apparent that on the basis of applicant's disclosure, an adequate written description of the invention defined by the claims requires more than a mere statement that it is part of the invention and reference to potential methods and/or molecular structures of molecules that are essential for the genus of a nucleic acid sequence encoding a polypeptide having NOS activity; what is required is the knowledge in the prior art and/or a description as to the availability of a representative number of species of biochemical or

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molecular structures of a nucleic acid sequence encoding a polypeptide having NOS activity that must exhibit the disclosed biological functions as contemplated by the claims.

Contemplating a genus of nucleic acids encoding a polypeptide having NOS activity is not sufficient to support the claimed genus of nucleic acids. The claimed invention as a whole is not adequately described if the claims require essential or critical elements, which are not adequately described in the specification and which is not conventional in the art as of applicant's effective filing date. Claiming unspecified polypeptides having NOS activity and/or a genus of a nucleic acid sequence that must possess the biological properties as contemplated by applicant's disclosure without defining what means will do so is not in compliance with the written description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)). Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. Pfaff v. Wells Electronics, Inc., 48 USPQ2d 1641, 1646 (1998). The skilled artisan cannot envision the detailed structure of a genus of a nucleic acid sequence encoding a polypeptide having NOS activity that must exhibit the contemplated biological functions, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the structures and/or methods disclosed in the as-filed specification. Thus, in view of the reasons set forth above, one skilled in the art at the time the invention was made would not have recognized that applicant was in possession of the claimed invention as presently claimed.

Claims 1-6 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of reducing portal hypertension in a mammal, comprising directly administering to a hepatic vein of said mammal a vector comprising a nucleic acid sequence encoding a nitric oxide synthase (NOS) polypeptide, and does not reasonably provide enablement for using a genus of nucleic acids and genus of administration routes in the claimed invention. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in In re Wands, 858 F.2d 731, 8USPQ2d 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The filed of the invention lies in a method of gene therapy for reducing portal hypertension in a mammal, wherein said method comprises administering a nucleic acid sequence encoding a NOS polypeptide under conditions such that the sequence is expressed and said reduction is observed.

Furthermore, and with respect to claims directed to any vector useful for gene therapy and directed to any therapeutic treatments of reducing portal hypertension in a mammal; the state

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of the art, exemplified Anderson et al., *Nature*, Vol. 392, pp. 25-30, 1998, displays major consideration for any gene transfer or any DNA therapy protocol involve issues that include:

- 1) The type of vector and amount of DNA constructs to be administered,
- 2) The route and time course of administration, the sites of administration, and successful uptake of the claimed DNA at the target site;
- 3) The trafficking of the genetic material within cellular organelles, the rate of degradation of the DNA, the level of mRNA produced, the stability of the mRNA product, the amount and stability of the protein produced, and
- 4) What amount of the expressed proteins considered to be therapeutically effective for a DNA therapy method.

In addition, all of these issues differ dramatically based on the specific vector used, the route of administration, the animal being treated, therapeutically effective amount of the DNA, and the disease being treated.

Anderson indicates that teaches that gene therapy is a powerful new technology that still requires several years before it will make a noticeable impact on the treatment of disease, and that several major deficiencies still exist including poor delivery systems, both viral and non-viral, and poor gene expression after genes are delivered (pp. 25-30).

Anderson further teaches that the reason for the low efficiency of gene transfer and expression in human patients is that we still lack the basis understanding of how vectors should be constructed what regulatory sequences are appropriated for which cell types (page 30, column 1, last paragraph). Furthermore, Verma, *Nature*, Vol. 389, pages 239-242, 1997, indicates that factors including the nature of the diseases and/or disorders, the nature of a DNA and/or target

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tissue, and a delivery system and/or amounts of the DNA complexes employed in the delivery system that would generate a therapeutic effect *in vivo* must be considered for any gene therapy method to be successful (page 238, columns 1 and 2). Thus, at the time the application was filed, gene therapy was considered unpredictable.

The specification contemplates that while the working examples use an adenoviral vector. Furthermore, the applicant provides two working examples which encompass: Example 1 comprises determining the ability of adenoviral vectors comprising the nucleic acid encoding the neuronal (nNOS) polypeptide to transduce hepatocytes, sinusoidal endothelial and stellate cells *in vitro* (pages 20-21). The adenovirus vectors efficiently transduced sinusoidal endothelial, stellate cells and hepatocytes. Next, the adenovirus was used to determine the effectiveness of *in vivo* gene transfer of nNOS by administering via the femoral vein to normal rats and rats with a liver injury (pages 21-22). The transduction rate of nNOS in the injured liver was less than that in normal livers. In addition, the data indicates that using the adenovirus can increase the NO production compared to control cells. Next, the experiment determined if the transduced NOS had biological and physiological effects on liver cells (pages 23-25). Portal pressure was measured in normal rats and rats having a liver injury. The adenovirus reduced portal pressure in treated animals compared to the control animals. Example 2 comprises of isolating cells from normal rats and transducing stellate, hepatocytes and sinusoidal endothelial cells with adenovirus containing either B-gal or nNOS (page 26 and Figure 5).

The specification and the art of record provide sufficient guidance for one skilled in the art to make and/or use a method of gene therapy for reducing portal hypertension in a mammal comprising directly administering to the mammal a vector comprising a nucleic acid sequence



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encoding a NOS gene. However, the specification does not provide sufficient guidance for one skilled in the art to make and use a replicant competent vector in a method of gene therapy for reducing portal hypertension. In addition to the doubts expressed by Verma and Anderson, the state of the art for using vectors for gene therapy as exemplified by Mountain (*Trends Biotechnol.* Vol. 18, pp. 119-128, 2000). Mountain teaches:

Gene transfer to somatic cells can take place in vivo (page 119, left column, 3<sup>rd</sup> paragraph). In vivo methods used several types of vectors (e.g. viral, non-viral, physical). The main disadvantage with viral vectors is insert-size limitation and immunogenicity (page 119, right column, 1<sup>st</sup> paragraph). Non-viral vectors give less efficient transfection especially in vivo) and more-transient expression (pages 119-120). Non-viral vectors giving efficient gene transfer in vivo are not yet available (page 125, right column, 3<sup>rd</sup> paragraph). Mountain further states that “integrating vectors, and perhaps most non-integrating vectors, transgene expression appears to be limited and usually silenced by incorporation into condensed and transcriptionally inactive chromatin, both in vivo (page, 125, right column, 1<sup>st</sup> paragraph).

Replication competent vectors are problematic because the replicant competent vector can result in cytotoxicity to target cells due to the accumulation of viral proteins, which is toxic to mammalian cells. Thus, gene therapy, replication incompetent or replication defective (transgene-containing) adenovirus genomes are preferred over replication competent forms.

Since, it is known in the art that efficient delivery of therapeutic gene and appropriate gene expression is crucial issues for clinically relevant gene therapy. In addition, gene therapy produces transient expression of the therapeutic gene, which requires additional treatment. This

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additional treatment, results in an immune response in the mammal that results in unsuccessful expression of the therapeutic gene. Furthermore, the specification does not provide sufficient guidance for what would happen when the mammal that is deficient or null in the expression NOS is exposed to viral antigens, potential viral recombination, or an immunogenic novel protein (NOS). The disclosure does not provide sufficient guidance for how to circumvent the immune response in any mammal undergoing a method of gene therapy using a viral vector comprising a NOS gene. Thus, in view of the art of record and the specification, the disclosure does not provide sufficient guidance for using any vector comprising a nucleic acid sequence encoding a NOS polypeptide sequence other than a replicant competent viral vector.

Furthermore, the art of record and the specification do not teach how to use a genus of administration routes to target said cells and provide a therapeutic effect. Since nucleic acid or vector comprising the nucleic acid can transduce several different types of cells in a mammal, the specification does not teach one skilled in the art how to sufficiently target enough nucleic acid to the target cells using a genus of administration routes to produce gene expression at a therapeutic level. Thus, the claims do not commensurate with the teachings in the specification.

In conclusion, the specification and claims coupled with the art of record, at the time the invention, was made do not provide sufficient guidance and/or evidence to reasonably enable the full breadth of the claimed invention. Given that gene therapy wherein any carrier is employed to correct a disease or a medical condition in any mammal was unpredictable at the time the invention was made, and given the lack of sufficient guidance as to a gene therapy effect produced by any of the gene delivery vectors cited in the claims, one skilled in the art would

have to engage in a large quantity of undue experimentation in order to practice the claimed invention based on the applicant's disclosure and the unpredictability of gene therapy.

*Claim Rejections - 35 USC § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-7 are rejected under 35 U.S.C. 102(a) as being anticipated by Yu et al (Hepatology, Vol. 30, October 1999, 631). Yu uses an adenovirus vector containing rat neural nitric oxide synthase (nNOS) in a method of gene therapy for reducing portal hypertension in experimental rats by administering the vector via femoral vein.

Claims 1 and 3-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Fevery et al., (Digestion, Vol. 59, pp. 58-59, 1998). Fevery teaches a method of gene therapy for reducing portal hypertension comprising administering via portal vein an adenovirus vector comprising the gene encoding calcium-dependent constitutional enzyme (type III, ceNOS) to CCL4 cirrhotic rats (page 59).

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or non-obviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1 and 2 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fevery taken with either Channon et al (Cardiovascular Research, Vol. 32, pp. 962-972, 1996) or Yu et al (Hepatology, Vol. 30, October 1999, 631).

The rejection of the base claim 1 under 35 U.S.C. 102 is applied here as indicated above, by Fevery. However, Fevery does not specifically teach delivering a replicant defective viral vector comprising a nucleic acid sequence encoding a neuronal NOS polypeptide to a mammal for reducing portal hypertension.

However, at the time the invention was made, Yu teaches an adenovirus containing rat neural nitric oxide synthase (nNOS) was prepared and administered via femoral vein in rats undergoing bile duct ligation to reduce portal hypertension in rats (631).

In addition, at the time the invention was made, Channon teaches the production of an adenoviral vector comprising a nucleic acid sequence encoding the neuronal isoform of NOS (abstract) for use in transfected human vascular cells.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Fevery taken with Yu to use an adenovirus vector comprising the neuronal NOS as taught by Yu in a method of gene therapy for reducing hypertension in a mammal. One of ordinary skill in the art would have been motivated to use the adenovirus vector in the gene therapy method because of the results displayed by Yu for reducing hypertension in a mammal by using the adenovirus vector.

In addition, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made, as a matter of designer's choice, to combine the teaching of Fevery taken with Channon to produce a vector comprising a nucleic acid sequence encoding a neuronal NOS polypeptide and delivering the vector to a mammal for a method of reducing portal hypertension in the mammal. It would have been a matter of design choice to one of ordinary skill in the art to use any NOS polypeptide because, evidence to the contrary of an

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unexpected property of using neuronal NOS, any nucleic acid encoding an isoform of NOS could be used for expressing NOS in the liver at a level that a reduction in portal hypertension would be observed in said mammal, in particularly in view of the results displayed by Fevery. In addition, using the adenoviral vector produced by Channon would save time in producing a vector comprising a nucleic acid sequence encoding the neuronal polypeptide because the vector was already produced and tested.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Claims 1 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fevery taken with either Freidman et al (Nutr. Clin. Pract. Vol. 9, pages 69-72, 1994) or Yu et al. (Hepatology, Vol. 30, October 1999, 631).

The rejection of the base claim 1 under 35 U.S.C. 102 is applied here as indicated above, by Fevery. However, Fevery does not specifically teach delivering a replicant defective adenoviral vector via the femoral vein to a mammal for reducing portal hypertension.

However, at the time the invention was made, Yu teaches an adenovirus containing rat neural nitric oxide synthase (nNOS) was prepared and administered via femoral vein in rats undergoing bile duct ligation to reduce portal hypertension in the rats (631).

In addition, at the time the invention was made, Friedman teaches that femoral venous catheters (FVCs) is a safe and effective alternative to other forms of central venous access for delivering a substance to a mammal.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Fevery and Yu to use the femoral vein to deliver the recombinant viral vector to the mammal's liver for a method of reducing portal hypertension. One of ordinary skill in the art would have been motivated to use the femoral vein to deliver the vector because the route of delivery was well known in the art for delivering an adenoviral vector to a rat, as taught by Yu.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Fevery taken with Friedman to use the femoral vein to deliver the recombinant viral vector to the mammal's liver for a method of reducing portal hypertension. One of ordinary skill in the art would have been motivated to use the femoral vein to deliver the vector because the route of delivery was well known in the art for delivering a therapeutic substance to a mammal.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Claims 1 and 3-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Varenne et al. (US 6,398,757) taken with Fevery et al., (Digestion, Vol. 59, pp. 58-59, 1998). Varenne teaches gene therapy for blood vessel associated disorders using an adenovirus comprising NOS (columns 2 and 14). However, Varenne does not specifically teach using the method to treat portal hypertension in a patient.

However, at the time the invention was made, expressing NO synthase in the liver can be used to treat portal hypertension as exemplified by Fevery (page 58). Fevery teaches the portal hypertension is a major complication of cirrhosis and several other liver diseases (page 58).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Varenne taken with Fevery, namely to use the method taught by Varenne to treat portal hypertension. One of ordinary skill in the art would have been motivated to combine the teaching because expressing NOS in the liver of a patient with portal hypertension can treat portal hypertension.

In addition, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Varenne taken with Fevery, namely to use the method taught by Varenne to treat a patient with cirrhosis. One of ordinary skill in the art would have been motivated to combine the teaching because portal hypertension is a major complication of cirrhosis and expressing NOS in the liver of a patient with portal hypertension resulting from cirrhosis can treat portal hypertension caused by cirrhosis.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (571) 272-0764. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.



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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, acting SPE – Art Unit 1635, can be reached at (571) 272-0811.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 O.G. 30 (November 15, 1989). The CM1 Fax Center number is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Brian Whiteman  
Patent Examiner, Group 1635

